

**REMARKS**

Claims 1-3 and 5-9 are pending in this application. By this Amendment, claims 1-3 and 5-9 are amended and claim 4 is cancelled. Support for the amendments to claims 1-3 and 5-9 can be found, for example, in original claims 1-9. No new matter is added. In view of the foregoing amendments and following remarks, reconsideration and allowance are respectfully requested.

**Objection to Specification**

The Office Action objects to the specification. By this Amendment, the specification is amended in accordance with the helpful suggestions in the Office Action. Accordingly, withdrawal of the objection is respectfully requested.

**Claim Objection**

The Office Action objects to claim 2. By this Amendment, claim 2 is amended in accordance with the helpful suggestion in the Office Action. Accordingly, withdrawal of the objection is respectfully requested.

**Rejection Under 35 U.S.C. §112, Second Paragraph**

The Office Action rejects claims 5 and 8 as indefinite under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse the rejection.

The Office Action asserts that claim 5 is indefinite for reciting "a 64<sup>th</sup> amino acid of apomyoglobin." By this Amendment, claim 5 is amended to remove the reference to "a 64<sup>th</sup> amino acid of apomyoglobin," rendering the rejection moot as to claim 5.

The Office Action asserts that claim 8 is indefinite for reciting "and two carbons included in benzene rings." By this Amendment, claim 8 is amended to recite that the variable J comprises "two adjacent carbon atoms in a benzene ring." Applicants submit that this recitation is definite.

For the foregoing reasons, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §112, First Paragraph

The Office Action rejects claims 1-9 under the enablement requirement of 35 U.S.C. §112, first paragraph. Claim 4 is cancelled, rendering the rejection moot as to that claim. As to the remaining claims, Applicants respectfully traverse the rejection.

By this Amendment, claim 1 is amended to recite "[a] metal complex-protein composite, comprising an apoprotein having a cavity and a metal complex, wherein: the apoprotein is selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants; the metal complex is prepared by complexation of a metal ion with a ligand; the metal ion is selected from the group consisting of rhodium, ruthenium, and palladium; the metal complex-protein composite has a structure such that the metal complex is received in the cavity of the protein; the metal complex is selected such that the metal complex does not cause degradation or instability of the apoprotein; and amino acid residues of the apoprotein coordinate with the metal complex" (emphasis added). The Office Action indicates that such a claim is enabled by the instant specification. *See* Office Action at page 3, last paragraph. Claims 2, 3 and 5-9 are rejected solely for their dependency from claim 1.

For the foregoing reasons, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §102

The Office Action rejects claims 1-4 under 35 U.S.C. §102(b) over Jackson et al., "Placement of Ru(BPY)<sub>2</sub><sup>2+</sup> In the Heme Pocket of Cytochrome B<sub>5</sub>," Book of Abstracts, ACS National Meeting, San Francisco, CA, March 26-30, 2000, Abstract 510 (2000) ("Jackson").

Claim 4 is cancelled, rendering the rejection moot as to that claim. As to the remaining claims, Applicants respectfully traverse the rejection.

As indicated above, claim 1 recites "[a] metal complex-protein composite, comprising an apoprotein having a cavity and a metal complex, wherein: the apoprotein is selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants ..." (emphasis added). Jackson does not teach or suggest such metal complex-protein composite.

The Office Action asserts that Jackson discloses a metal complex protein comprising cytochrome protein complexed with ruthenium, the ruthenium being complexed with bipyridine (bpy). Notwithstanding this assertion, Jackson does not anticipate and would not have rendered obvious the metal complex-protein composite of claim 1.

Claim 1 requires a metal complex-protein composite including an apoprotein selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants. There is absolutely no teaching or suggestion in Jackson of a metal complex-protein composite including an apoprotein selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants. Jackson's teachings are strictly limited to a metal complex-protein composite including an apocytochrome. As Jackson does not teach or suggest a metal complex-protein composite including an apoprotein selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants, Jackson does not teach or suggest each and every element of claim 1.

Claim 1 is not anticipated by Jackson. Claims 2 and 3 depend from claim 1 and, thus, also are not anticipated by Jackson. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §103

The Office Action rejects claims 1-4 and 6-8 under 35 U.S.C. §103(a) over Jackson in view of Smolenski et al., "New Rhodium(III) and Ruthenium(II) Water-Soluble Complexes with 3,5-Diaza-1-methyl-1-azonia-7-phosphatricyclo[3.3.1.1<sup>3,7</sup>]decane," *Inorganic Chemistry*, 42(10): 3318-22 (2003) ("Smolenski") and Cadierno et al., "Ruthenium(II) and Ruthenium(IV) Complexes Containing  $\kappa^1$ -P-,  $\kappa^2$ -P,O-, and  $\kappa^3$ -P,N,O-Iminophosphorane-Phosphine Ligands  $\text{Ph}_2\text{PCH}_2\text{P}\{\text{=NP(=O)(OR)}_2\}\text{Ph}_2$  (R = Et, Ph): Synthesis, Reactivity, Theoretical Studies, and Catalytic Activity in Transfer Hydrogenation of Cyclohexanone," *Inorganic Chemistry*, 42(10): 3293-3307 (2003) ("Cadierno"). Claim 4 is cancelled, rendering the rejection moot as to that claim. As to the remaining claims, Applicants respectfully traverse the rejection.

Claim 1 is set forth above. Jackson fails to teach or suggest each and every feature of claim 1 at least for the reasons discussed above. Smolenski and Cadierno do not remedy the deficiencies of Jackson.

The Office Action does not contend that Jackson teaches or suggests a metal complex-protein composite including an apoprotein selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants. The Office Action does assert, however, that it would have been obvious to substitute metal/phosphino complexes disclosed in Smolenski and Cadierno for the ruthenium/bipyridine complex in the a metal complex-apocytochrome composite disclosed in Jackson.

Jackson discloses a composite including a specific apoprotein derived from cytochrome b<sub>5</sub> and a specific metal complex,  $\text{Ru}(\text{bpy})_2^{2+}$ . There is no teaching or suggestion in Jackson of a metal complex-protein composite including any apoprotein other than the specific apocytochrome derive from cytochrome b<sub>5</sub>. Smolenski and Cadierno disclose

specific metal complexes. However, there is no teaching or suggestion in Smolenski or Cadierno that the disclosed metal complexes could or should be used with the apocytochrome disclosed in Jackson, much less with the specific apoproteins recited in claim 1. That is, one of ordinary skill in the art would not reasonably expect that the metal complexes disclosed in Smolenski and Cadierno would form viable composites with either the apocytochrome disclosed in Jackson or the specific apoproteins recited in claim 1. In fact, there is no reference in either Smolenski or Cadierno to proteins at all. The only teaching or suggestion that a metal complex-protein composite could be formed including an apoprotein selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants, is found in the instant specification. As is well settled, relying on the instant specification for motivation to combine the cited references would constitute impermissible hindsight. *See, e.g.*, MPEP §2143 ("The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure") (citing *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991)).

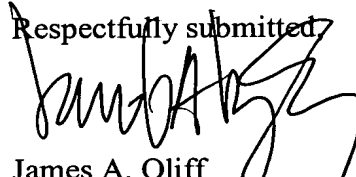
As none of Jackson, Smolenski and Cadierno teaches or suggests a metal complex-protein composite including an apoprotein selected from the group consisting of apomyoglobin, apohemoglobin, apoheme oxygenase, apocatalase, apoferritin, and their variants, the combination of references fails to teach or suggest each and every element of claim 1.

Claim 1 would not have been rendered obvious by Jackson, Smolenski and Cadierno. Claims 2, 3 and 6-8 depend from claim 1 and, thus, also would not have been rendered obvious by the cited references. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1-3 and 5-9 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,  
  
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